

**DOCKET NO: UPAP0025-100 (K1763)**  
**PATENT APPLICATION**

**Serial No.: 09/719,067**  
**Filed: August, 16 2001**

**IN THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

Please cancel claim 3.

Please amend claims 11 and 31.

**STATUS OF CLAIMS**

**Claim 1. (currently amended)** A method of delivering a protein to a macrophage cell or a cell of macrophage derived lineage of an individual comprising the steps of:

administering to said individual at a site on said individual's body, a DNA molecule, wherein said DNA molecule is a plasmid comprising a nucleotide sequence that encodes said protein, wherein said DNA molecule is operably linked to a macrophage specific promoter and a polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage, wherein said DNA molecule is taken up by a macrophage cell and/or a cell of macrophage derived lineage where said nucleotide sequence is expressed to produce said protein in said macrophage cell and/or said cell of macrophage derived lineage.

**Claim 2 (original)** The method of claim 1 wherein said DNA molecule is administered by a route of administration selected from the group consisting of: intradermal, subcutaneous, intraperitoneal, intramuscular, and oral.

**Claim 3 (canceled)**

**Claim 4 (canceled)**

**DOCKET NO: UPAP0025-100 (K1763)**  
**PATENT APPLICATION**

**Serial No.: 09/719,067**  
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**Claim 5 (previously presented)** A method of delivering a protein to a macrophage cell or a cell of macrophage derived lineage of an individual comprising the steps of:

administering to said individual at a site on said individual's body, a DNA molecule comprising a nucleotide sequence that encodes said protein, wherein said DNA molecule is operably linked to a macrophage specific promoter and a polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage, wherein said macrophage specific promoter is selected from the group consisting of a catalase promoter, a CD156 promoter, a M-CSFR promoter, a p73 promoter, and an FcγRI promoter, wherein said DNA molecule is taken up by a macrophage cell and/or a cell of macrophage derived lineage where said nucleotide sequence is expressed to produce said protein in said macrophage cell and/or said cell of macrophage derived lineage.

**Claim 6 (original)** The method of claim 1 wherein said polyadenylation signal is selected from the group consisting of: an SV40 polyadenylation signal and a bovine growth hormone polyadenylation signal.

**Claim 7 (original)** The method of claim 1 wherein said DNA molecule is administered with a composition which facilitates uptake of said DNA molecule by a cell.

**Claim 8 (original)** The method of claim 1 wherein said DNA molecule is administered with bupivacaine.

**Claim 9. (previously presented)** A method of delivering a protein to a lymphnode of an individual comprising the steps of:

- a) identifying said lymphnode that is to have protein delivered to;
- b) locating a site on said individual's body that is proximal to said lymphnode;
- c) administering to said individual at said site, a DNA molecule comprising a nucleotide sequence that encodes said protein, wherein said DNA molecule is operably

DOCKET NO: UPAP0025-100 (K1763)  
PATENT APPLICATION

Serial No.: 09/719,067  
Filed: August, 16 2001

linked to a promoter and a polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage,

wherein said DNA molecule is taken up by a macrophage cell and/or a cell of macrophage derived lineage where said nucleotide sequence is expressed to produce said protein in said macrophage cell and/or said cell of macrophage derived lineage, and said macrophage cell and/or said cell of macrophage derived lineage drains to said lymphnode, and delivers said protein in said lymphnode.

Claim 10 (original) The method of claim 9 wherein said DNA molecule is administered by a route of administration selected from the group consisting of: intradermal, subcutaneous, intraperitoneal, intramuscular, and oral.

Claim 11 (currently amended) ~~The method of claim 9~~ A method of delivering a protein to a lymphnode of an individual comprising the steps of:

- a) identifying said lymphnode that is to have protein delivered to;
- b) locating a site on said individual's body that is proximal to said lymphnode;
- c) administering to said individual at said site, a DNA molecule, wherein said DNA molecule is a plasmid, comprising a nucleotide sequence that encodes said protein, wherein said DNA molecule is operably linked to a promoter and a polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage,

wherein said DNA molecule is taken up by a macrophage cell and/or a cell of macrophage derived lineage where said nucleotide sequence is expressed to produce said protein in said macrophage cell and/or said cell of macrophage derived lineage, and said macrophage cell and/or said cell of macrophage derived lineage drains to said lymphnode, and delivers said protein in said lymphnode.

Claim 12 (original) The method of claim 9 wherein said promoter is a macrophage promoter.

**DOCKET NO: UPAP0025-100 (K1763)**  
**PATENT APPLICATION**

**Serial No.: 09/719,067**  
**Filed: August, 16 2001**

**Claim 13 (original)** The method of claim 9 wherein said promoter is selected from the group consisting of: an actin promoter, a CD11 promoter, a CD13 promoter, an MHC-I promoter, an MHC-II promoter, a CD25 promoter, a CD80 promoter, a CD86 promoter, a catalase promoter, a CD156 promoter, an M-CSFR promoter, a p73 promoter, an FcγRI promoter, a CMV promoter, an actin promoter, an SV40 promoter and a Malony virus promoter.

**Claim 14 (original)** The method of claim 9 wherein said polyadenylation signal is selected from the group consisting of: an SV40 polyadenylation signal and a bovine growth hormone polyadenylation signal.

**Claim 15 (original)** The method of claim 9 wherein said DNA molecule is administered with a composition which facilitates uptake of said DNA molecule by a cell.

**Claim 16 (original)** The method of claim 9 wherein said DNA molecule is administered with bupivacaine.

**Claim 17 (original)** The method of claim 9 wherein said protein comprises a secretion signal sequence.

**Claim 18 (previously presented)** A method of inducing an immune response against an immunogen in an individual comprising the step of:

administering to said individual at a site on said individual's body, a DNA molecule comprising a nucleotide sequence that encodes said immunogen operably linked to a macrophage specific promoter and a polyadenylation signal that are functional in macrophage cells and/or cells of macrophage derived lineages,

wherein said DNA molecule is taken up by a macrophage cell and/or a cell of macrophage derived lineage where said nucleotide sequence is expressed to produce said

**DOCKET NO: UPAP0025-100 (K1763)**  
**PATENT APPLICATION**

**Serial No.: 09/719,067**  
**Filed: August, 16 2001**

immunogen in said macrophage cell and/or said cell of macrophage derived lineage and an immune response mediated by said macrophage is generated against said immunogen.

**Claim 19 (previously presented)** The method of claim 18 wherein said DNA molecule further comprises

a nucleotide sequence that encodes an immunomodulating protein, wherein said DNA molecule is operably linked to a promoter and a polyadenylation signal that are functional in macrophage cells and/or cells of macrophage derived lineages, and/or

a second DNA molecule is additionally administered to said site on said individual's body, said second DNA molecule comprising a nucleotide sequence that encodes an immunomodulating protein, wherein said second DNA molecule is operably linked to a promoter that is functional in macrophage cells and/or cells of macrophage derived lineages and a polyadenylation signal that is functional in macrophage cells and/or cells of macrophage derived lineages.

**Claim 20 (original)** The method of claim 18 wherein said immune response targets a pathogen.

**Claim 21 (original)** The method of claim 18 wherein said immune response is a protective immune response.

**Claim 22 (original)** The method of claim 18 wherein said immune response is a therapeutic immune response.

**Claim 23. (previously presented)** A method of modulating an individual's immune system comprising the step of:

administering to said individual at a site on said individual's body, a DNA molecule comprising a nucleotide sequence that encodes an immunomodulating protein, wherein said DNA molecule is operably linked to a macrophage specific promoter and a

**DOCKET NO: UPAP0025-100 (K1763)**  
**PATENT APPLICATION**

**Serial No.: 09/719,067**  
**Filed: August, 16 2001**

polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage,

wherein said DNA molecule is taken up by a macrophage cell and/or a cell of macrophage derived lineage where said nucleotide sequence is expressed to produce said immunomodulating protein modulates said individual's immune system.

**Claim 24. (previously presented)** The method of claim 23 wherein said DNA molecule further comprises

a nucleotide sequence that encodes an immunomodulating protein, wherein said DNA molecule is operably linked to a promoter and a polyadenylation signal that are functional in macrophage cells and/or cells of macrophage derived lineages and/or

a second DNA molecule is additionally administered to said site on said individual's body, said second DNA molecule comprising a nucleotide sequence that encodes an immunomodulating protein, wherein said second DNA molecule is operably linked to a promoter that is functional in macrophage cells and/or cells of macrophage derived lineages and a polyadenylation signal that is functional in macrophage cells and/or cells of macrophage derived lineages.

**Claim 25. (previously presented)** A method of eliminating cells in a lymphnode of an individual comprising the step of:

administering to said individual at a site on said individual's body, a DNA molecule comprising a nucleotide sequence that encodes a cytotoxic protein, wherein said DNA molecule is operably linked to a promoter and a polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage,

wherein said DNA molecule is taken up by a macrophage cells and/or a cells of macrophage derived lineage where said nucleotide sequence is expressed to produce said protein in said macrophage cells and/or said cells of macrophage derived lineage,

said macrophage cell and/or a cell of macrophage derived lineage secretes or releases said cytotoxic protein in said lymphnode eliminating cells in said lymphnode.

**DOCKET NO: UPAP0025-100 (K1763)  
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**Claim 26 (original)** The method of claim 25 wherein said protein comprises a secretion signal sequence.

**Claim 27 (original)** The method of claim 25 wherein said protein is a toxin.

**Claim 28 (original)** The method of claim 25 wherein said protein is ricin A chain or diphtheria toxin.

**Claim 29. (previously presented)** A method of delivering a desired protein to an individual comprising the step of:

administering to said individual at a site on said individual's body, a DNA molecule comprising a nucleotide sequence that encodes said desired protein, wherein said DNA molecule is operably linked to a macrophage specific promoter and a polyadenylation signal that are functional in a macrophage cell and/or a cell of macrophage derived lineage,

wherein said DNA molecule is taken up by a macrophage cells and/or a cells of macrophage derived lineage where said nucleotide sequence is expressed to produce said desired protein in said macrophage cells and/or said cells of macrophage derived lineage.

**Claim 30. (previously presented)** The method of claim 25 wherein said promoter is a macrophage specific promoter.

**Claim 31. (currently amended)** ~~The method of claim 25~~ A method of eliminating cells in a lymphnode of an individual comprising the step of:

administering to said individual at a site on said individual's body, a DNA molecule, wherein said DNA molecule is a plasmid, comprising a nucleotide sequence that encodes a cytotoxic protein, wherein said DNA molecule is operably linked to a promoter and a polyadenylation signal that are functional in a macrophage cell and/or a

**DOCKET NO: UPAP0025-100 (K1763)**  
**PATENT APPLICATION**

**Serial No.: 09/719,067**  
**Filed: August, 16 2001**

cell of macrophage derived lineage, wherein said DNA molecule is taken up by a macrophage cells and/or a cells of macrophage derived lineage where said nucleotide sequence is expressed to produce said protein in said macrophage cells and/or said cells of macrophage derived lineage, said macrophage cell and/or a cell of macrophage derived lineage secretes or releases said cytotoxic protein in said lymphnode eliminating cells in said lymphnode.